

CATGGTAGACGGCTGGCCGGAGGGACAGGGCTGAGACCGGCATGGACCGCAAACCATGGTAGCAATGGGGCGCAAGGCCGGAGGGGCTCTCAGGACTTCGGCGGGACTCAAGTACAACCTCCCGCTAGAGAACATGAATGGCTTGAGGAGGGTGTGGA  
GTTCCCTGCCTGCGAACAAATGCCAAGAAAGTGGAGAACGGGCCCCAGGCCTGGGTGGCTGGCAGTGTGTCAGCTTCTCCTCTGCTCTCCATGGCTGGCTGTGGACTTCCATTATCGGAATGTGCCGGTTCAAAAGTCTCAATGCCATCTG  
AGGATCACAAATGAGATCTTCTGGATCGCTGAGAACCTCCACAGAGTTATCAGGCCGGCCAGCAGGTGAAGGAGGCCGGAGCTGAGCTGCTGAGTCAACAGTCCCTGGCTTCCAGTGGAGGGCAGTGTCA  
TCGCCTACTACTGGTCAGAGTTCAGCATCCCCACACCTGGCAGAACAGGTTGATCGGCCATGGCTGTGGAGCTGAGGAGGAGCTGAGTGTGACACAGGAGGAGCTGAGTGTAA  
TTGCCACCCGAGCACGGGACTGAAATCCTCGTCAACATCTGTGGTGGCTTCCCATTGACCCAGAACATGCTGCAGAGGAC  
TCAGGACAAACAGCTGAGTTTGGCTGCATGCCATGGTCAGCAGTGCACAGCTCACTACCCCTGGCTTCCCAACAGTCCCT  
ACCCGGCCATGCCCTGCCAGTGGGCTCGGGGGAGCGCGACTCTGTGCTGAGCCTCACCTCCGAAGCTTGTGATGTCGCT  
CCCTGTGATGAGCATGGCAGTGCACCTGGTACCGTGTATGATAGCCTGAGCCCATGGAACCCACGCTGTGGTGCAGGCTGTGG  
CACCTCTCACCCCTACAACCTGACTTCTCTCCAGAACGCTCTCTGTCACGCTGATAACCAAACTGACGGGCGAC  
ATCCCTGGCTTGAGGCCACTTCTCCAGCTGCCAACAGATGAGCAGCTGAGGGCTTTTGAGTGAACACCAAGGGACATTAGC  
AGCCCTACTATCCAGGCCACTCCGCCAACATCAACTGCACATGGAATATCAAGGTGCCAACACCGAACGTGAAGGTGCG  
CTTCAAACCTCTCTATCTGGTGAGCCCCAACGTTACCGAGTGGGCTCTGCACCAAGGACTATGTGAGATCAACGGGGAGAACGACT  
GGGGTGAAGAGGTCCCAAGTTGTGGTGAACAGCACAGCAGAACAGATTACAGTCCACTTCCATTCTGATCACTCGTACACGGACACC  
GGGTTCTAGCTGAGTACCTCTCTACAGTCTCAAGGACCCCGTGGCCAGGGATGTTCATGTGCAAGACTGGACGGTGCACTCCGAAA  
GGAACGGCTCGCCTGCCAGGGCAGATGCCGGATTATAGTGTGAGCGTTACTGCCGATGCCAACCCACCGACTTCACGT  
GCAAAACCACTCTGCAAGCCCCCTCTCTGGCTCTGTGACAGTGTCAACGACTGTGGGGAGCGAACGTGACAGGAGGGCTGCAGC  
TGTCTGCTGGAGTTCAAGTGTTCATGGAAGTGTCTCCCTCAGAGCAGAACAGTGAATGGAAGGACAACGTGAGATGG  
GTCTGACGGGCTCATGTGACAGCGTGAATCTGCTCTTGACCAAAATATACTACCCGCTCCAAAATGGGCTCTGTCAGGCA  
AGGGCAACCCCTGAGTGTGATGGGAAGACGGACTGTAGCGATGGCTCCGATGAGAAAAACTGTGACTGTGGGCTGCGATCCTTAC  
AAACAGGCTCGCGTGGTTGGTGGCACGAATGCGGACAGGGCAGTGGCCCTGGCAGGTGAGGCCCTCCACGCCCTGGCCAGGGCCA  
CTTGTGTGGGCTCGCTCATCTCCTGACTGGCTGTGTCAGCTCATGCTTTCAGGATGACAAAAAATTCAAGTACTCAG  
ACTACACAGATGTGGACGGCTTCTGGTCTGTGGACCAAGAACGGCAGTGCCTCTGGGTGCAAGGAGCTGAAGCTCAAACGT  
ATCATCACCCACCCCTCTTCATGATTTACCTCGACTATGACATGCCCTGCTGGAGCTGGAGAACGTGGAGTACAGCAG  
CGTCTGCGCCCATCTGCTGCTGACTACCCATGCTTCCCTGCTGGCAAGGGCAGTCTGGTACAGGCTGGGGCAGACACAA  
AAGAGGGAGGTACCGAGCGCTGATCCTGCAAGGGAGATCCGTGTCATCAACCAAGACCACCTGTGAGGACCTCATGCCGAG  
CAGATCACCCACGAATGATGTGTGGGTTCTCTGAGCTGGGTGTGACTCTGCCAGGGTACTCTGGGGCCCTTGTCAAG  
CGCGGAGAAAGATGGCGAATGTCCAGGCTGGTGTGGTAGCTGGGTGAAGGCTGCGCTCAGAGAACGCCAGGGCTGTACA  
CAAGGCTCCCTGAGTGTGGACTGGATCAAAGAACGACACTGGGGTATAGCAGCAGTGGACAGACAGGCCACAAACACCCACAG  
GGATGCCGACATGCACACCTGGATACAGGAGAGGAACACTGACGACACATTATGCTGTGGCTCCCCCCCCAACACAAACCCAGAC  
TGTGAACGTGACATCCTTAGGACTCAGAGTTCTCCAAAGTGGGACCCCTCAAGAGTGGAGAGAGAACCTGGGTGCTAGCGGCCA  
GCCTGGGGCAAGGGTTGATGCCAGGCCCTCCCCCTAGCCCTGAGCTGGGTGAAGATGATGCTGTCCGGAGAGCTGCTTCAA  
CTGTCATTGAGCTCCGGAGCCATGGGAGGGCTCAGGGTACTCTTTCAAGGAAGCGCCAGGCCCTAGGAACCCAGAAA  
AGAGTGGTACCTAAGGCTGAAATTGTTGCTGTCAGGGGTGGTATTGAGAGTAAACATTATTTCTTTAAAAAAA  
AAAAAAAAA (SEQ ID NO:1)

MGSNRGRKAGGGSQDFGAGLKYNRSRLENMNGFEEGVFLPANNA  
KKVEKRGPRRVVVLVAVLFSFLLLSLMAGLLWVHFHYRNVRVQKVFNGLRLITNEIFL  
DAYENSTSTEFISLASQVKEARLKLLYNEVPVLGPYHKSAVTAFSEGSVIAYYWSSEFS  
I PPHLAAEVDRAMAVERVVTLPVRARALKSFVLTSVVAFPIDPRMLQLRTQDNSCSFAL  
HAHGAATVTRFTTPGFPNSPVYPAHARCVQWLRLGDDASVLSLTFRSFDVAPCDEHGSIDLV  
TVYDLSLSPMEPAHVRLCGTFPSYNLTFLSSQNVLVTLTNTDRHPGEATFFQL  
PKMSSCGGFLSDTQGTFSPPYGPYPPNINCTWNIVPNNRNVKVRFKLFYLVDPNV  
PVGSCTKDYVBEINGEKYCGERSQFVVSSNSKITYVHFHSHDHSYTDGFLAEYLSDSN  
DPCPGFMCKTGRCIRKELCDGWADCPDYSDERYCRCNATHQFTCKNQFCCKPLFWC  
DSVNDCGDGSDEEGCSCPAGSFKCSNGKCLPQSQKCNKGDKNCGDGSDEACDSVNVS  
CTKYTYRCQNLGLCSKGNPEDGKTDCCSDGSDEKNCDCGLRSFTKQARVVGGTNADEG  
EWPWQVSILHALGQHGLCGASLISPDLVLSAACHCFQDDKMFYKSODYTMWTAFLGLLDQS  
KRSASGVQELKLKRRIITHPSFNDFTFYDIALLELEKSVEYSTVVRPICLDPATHVFP  
AGKAIWVTGWGHTKEGGTGALILQKGEIRVINQFTCEDLMPQQITPRMMCVGFLSGGV  
DSCQGDSSGGPLSSAEKDGRMFQAGVVWSWGECAQRNKPGVYTRLPVVRDWIKEHTGV  
(SEQ ID NO: 2)

## FIGURE 1

underlined = deleted in targeting construct

[ ] = sequence flanking Neo insert in targeting construct

CATGGTAGACGGCTGCCCGGAGGGACCACGCGTCTGAGACCGGCATCGGACCGCCAAAA  
 CCATGGGTAGCAATCGGGCGCAAGGCCGGAGGGCTCTCAGGACTTCGGCGCGGGAC  
 TCAAGTACAACCTCCCGCTAGAGAACATGAATGGCTTGAGGAGGGTGTGGAGTTCTGC  
 CTGCGAACAAATGCCAAGAAAGTGGAGAACGAGGCCAGGCCTGGCTGGCTGGACTGG  
 CAGTGCCTGTCAGCTCCCTCTGCTCTCCATGGCTGGCTGGCTGGACTGGCACTTCC  
 ATATCGGAATGCGGGTCAAAGCTTCAATGGCATCTGAGGATCACAAATGAGA  
 TCCTCTGGATGCGTATGAGAACCTCCACAGGATTTACAGGCTGGCCAGGCCAGG  
 TGAGGAGGCCTGAAGCTGCTGACATGAAGTCCCTGTCTGGGTCACACAAGA  
 AGTCGGCTGTAACGCCCCACTGAGGGCAGTGTACAGGCTACTACTGGTCAGAGTTCA  
 GCATCCCCCACACCTGGCAGAAGAGGTTGATCGCGCCATGGCTGGAGCGAGTTGAA  
 CATTGCCACCCGAGCACGGCACTGAAATCTTCGTGCTAACATCTGTGGTGGCCTTCC  
 CCATTGACCCCAGAACATGCTGAGGGACTCAGGAAACACAGCTGCACTGGCTGGCAGT  
 CCCATGGTCAGTCAGTACACGCTTCACTACCCCTGGCTCCCAACAGTCCCTACCCGG  
 CGCATGGCCCTGCGAGTGGGCTCGGGGGACGCCACTCTGCTGAGCCTCACCT  
 TCCGAAGCTTGTGTCGCTCCCTGTGATGAGCATGGCAGTGACCTGGTCACCGTGTATG  
 ATAGCCTGAGCCCCATGGAACCCCACGCTGGTGCAGGCTGTGGCACCTTCACCC  
 CCTACAACCTGACTTTCTCTCCCTCCAGAACGCTTCTCTGTCAGCCTGATAACCAATA  
 CTGACCGGGCAGACATCCTGGCTTGAGGCCACTTCTCTCAGCTGCCAACAGATGAGCAGCT  
 GTGGCGGCTTTGAGTGAACACCAAGGGACATTAGCAGCCCTACTATCCAGGCCACT  
 ACCCGCCCAACATCAACTGCAATGGAATATCAAGGTGCCAACACCGGAACGTGAAGG  
 TGCCTTCAACTCTCTATCTGGGACCCCAACGTAACGCTGGCTCCTGCAACCAAGG  
 ACTATGTGGAGATCAACGGGGAGAAACTACTGCGGTGAGAGGTCCACTTGTGGTGA  
 GCAACAGCAGCAAGATTACAGTCCACTCCATTCTGATCACTCGTACACGGACACCGGGT  
 TCCTAGCTGAGTACCTCTCACGACTCCAACGACCCGTGCCAGGGATGTTCATGTGCA  
 AGACTGGACGGTGCATCGGAAGGAAACTGGCCTGGCAGGGCAGACTGCCCGGATT  
 ATAGTGTGAGCGTACTGCGATGCAATGCCACCCACAGTTCACGTGCAAAAACCGT  
 TCTGCAAGCCCCCTCTGGGTCTGTGACAGTGTCAACGACTGTGGGACGGAAAGTGACG  
 AGGAGGGCTGAGCTGCTCTGTGGAGTTCAAGTGTCCAATGGGAAGTGCTCCCTC  
 AGAGCCAGAAGTGTAAATGGGAAGGACAACGTGGAGATGGGTCTGACGAGGCTCATGTG  
 ACAGCGTGAATGCGTCTTGCACCAAATATACCTACCGCTGCCAAAATGGCTCTGTC  
 TGAGCAAGGGCAACCCCTGAGTGTGATGGGAAGACGGACTGTAGCGATGGCTCGATGAGA  
 AAAACTGTGACTGTGGGCTGCGATCTTACACAAACAGGCTCGGTGGTTGGCAGCA  
 ATGGCGGACGGGGCAGTGGCCCTGGCAGGTGAGCCTCACGCCCTGGCCAGGGCCACT  
 TGTGTGGGCCCTCGCTCATCTCTCTGACTGGCTGGTCTGCACTGGCTATTGCTTT  
 ATGACAAAATTCAAGTACTCAGACTACACGATGTGGACGGCTTCTGGTCTGCTGG  
 ACCAGAGCAAGCGCAGTGCCTCTGGGTGCAAGGAGCTGAAAGCTCAAACGTATCATCACCC  
 ACCCTTCTCAATGATTACCTTCAGACTGACATGCCCTGCTGGAGCTGGAGAAGT  
 CGGTGGAGTACGACCCGTCGCGCCCATCTGCTGGCTGATGCTACCCATGCTTCC  
 CTGCTGGCAAGGCCATCTGGTCAGGCTGGGGCACACAAAAGAGGGAG[GTACCGGA  
 GCGCTGATCTGCAAGAAGGTGAGATCCGTGTCATCAACCAAGACCACTGTGAGGACCTC  
 ATGCCGAGCAGATCACCCACGAATGATGTTGTTGGGTTCTCAGTGGGGTGTGGAC  
 TCCTGC]CAGGGTGAACCTGGTGGCCCTTGTCAGCGCAGGAGAAAG[ATGGGCGAATGT  
 TCCAGGCTGGTGTGGTGAAGCTGGGACTGGATCAAAGAGCACACTGGGGTATACGACCATG  
 GACAGACAGGCCACAAACACCCACAGGGATGCCGACATGCACACCTGGATACAGGA  
 GAGGAACACTGACGACATTATGCTGTGGCTCCCCCCCCAACACAACCCAGACTGTGA  
 ACTGCATCCTTAGGACTCAGAGTTCTTCAAAGTGGACCCCTCAAGAGTTGGAGAGAG  
 AACTTGCGTGTAGCGGCCAGCTGGGGCAAGGGTTTGATGGCAGCCTCCCCCTCTA  
 GCCCTGAGCTGGGTGAAGATGATGCTGCTCCGGAGAGCTGCTTCAAAGTGTCAATTGAGCT  
 CCCGGGAGCCCTATGGGAGGGAGGGCTCAGGGTCACTCTTCAAGGAAGGCCAGCCCTA  
 GGAACCCCCAGAAAAGAGTGGTACCTAAGGCTGAAAT]TGTGTTGCTGTTGCCAGGGTGG  
 GTATTGAGAGTAAAACATTTATTCTTTAAAAAAAAAAAAAA

FIGURE 2A

**Gene Sequence Structure**

\*

2466 bp

Sequence Deleted

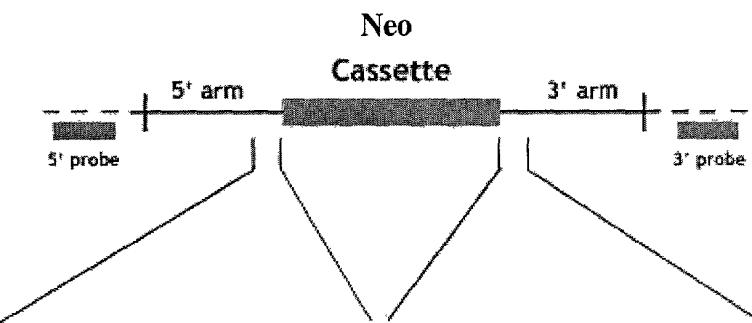
2505 bp

**Size of full-length  
cDNA:** 3106 bp


**Targeting Vector\*  
(genomic sequence)**

Construct Number: 2035

**Arm Length:**  
5': 3.8 kb  
3': 1 kb



5' >TTCCCCATTGAGACTGGCTTA  
CCCCGGAAGCTGCCTGCCTCAGTC  
TCCCGCTTCCGTCTCCCCAGGTA  
CCGGAGCGCTGATCCTGCAGAAGG  
GTGAGATCCGTGTCAATCAACCAGA  
CCACCTGTGAGGACCTCATGCCGC  
AGCAGATCACCCCACGAATGATGT  
GTGTGGGTTTCCTCAGTGGGGTG  
TGGACTCCTGC<3'  
(SEQ ID NO: 3)

5' >ATGGGCAGATGTTCCAGGCTG  
GTGTGGTGGGCTGGGGTGAAGGCT  
GCGCTCAGAGGAACAAGCCAGGCG  
TGTACACAAGGCTCCCTGTAGTTC  
GGGACTGGATCAAAGAGGCACACTG  
GGGTATAGCAGCATGGACAGACAG  
CCGACCACAAACACCCACAGGGAT  
GCCCGACATGCACACCTGGATACA  
GGAGAGGGACA<3'  
(SEQ ID NO: 4)

— Targeting Vector  
- - - Endogenous Locus

\* Not drawn to scale

**FIGURE 2B**